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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/858,279	05/15/2001	Theo Kirkland	TSRI 372.0 D2	3986

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EXAMINER	
HINES, JANA A	
ART UNIT	PAPER NUMBER
1645	7

DATE MAILED: 12/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/858,279	KIRKLAND ET AL.	
	Examiner	Art Unit	
	Ja-Na A Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 20-35* is/are pending in the application.

4a) Of the above claim(s) *14, 20 and 23-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 21-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 September 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 6 is acknowledged.

Amendment Entry

2. The amendments filed May 15, 2001 and February 21, 2002 have been entered. Claims 15-19 have been cancelled. The examiner acknowledges amendments to the specification. Claims 14, 20 and 23-35 are withdrawn from consideration. Claims 1-13 and 21-22 are under consideration in this office action.

Drawings

3. The drawings are objected to because of the reasons set forth in the attached PTOL-948. However, the corrections will not be held in abeyance and applicant must submit proposed drawing corrections in response to the requirement in the Office action.

Specification

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5-8 and 21-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for monoclonal antibodies 1E8, 2B5 and 18G4 that also inhibit LBP-mediated binding of LPS to CD14; monoclonal 2B5 that inhibits LBP-mediated LPS-dependent activation of myeloid cells; and monoclonal 2B5 that further inhibit LBP-mediated LPS-dependent secretion of tumor necrosis factor (TNF) from myeloid cells, does not reasonably provide enablement for any monoclonal antibody that inhibits LBP-mediated binding of LPS to CD14; monoclonals that inhibits LBP-mediated LPS-dependent activation of myeloid cells' or monoclonals that further inhibit LBP-mediated LPS-dependent secretion of tumor necrosis factor (TNF) from myeloid cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claims 5-6 are drawn to a monoclonal antibody that inhibits LBP-mediated binding of LPS to CD14. However example 2C of the specification at page 50 provides the determination of the effect of purified LBP and anti-LBP monoclonal antibodies on the binding of LPS to CD14. Only monoclonal antibodies 1E8, 2B5 and 18G4 were

shown to demonstrate inhibition of binding of LPS by Cd14-expressing CHO cells by either or both methods.

Dependant claim 7 recites a monoclonal that inhibits LBP-mediated LPS-dependent activation of myeloid cells while dependant claim 8 requires that the monoclonal further inhibit LBP-mediated LPS-dependent secretion of tumor necrosis factor (TNF) from myeloid cells. The specification appears to fail to recite specifically which antibodies meet this limitation. The claims are not limited to claiming only Mab 2B5. Mab 2B5 was the only monoclonal antibody shown to block the release of TNF when compared to assays performed without any antibody or with Mab 8F5 which was shown not to block LPS transfer to CD14. Applicant is broadly claiming a monoclonal antibody having the recited properties, but has only provided evidence of a single example. Moreover, Applicants other monoclonal antibodies do not have the recited properties. Based on the disclosure showing the other monoclonal antibodies which specifically bind LBP having different properties and characteristics than the claimed Mab 2B5, applicant is not enabled to the breadth of the claim with only a single working example.

No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict whether the detection will or will not occur. Accordingly, one of skill in the art would be required to perform undue experimentation to find monoclonal antibodies that have the recited properties when the specification clearly teaches that only a few antibodies have the recited properties. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

6. Claims 1-13 and 21-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a deposit rejection.

The specification lacks complete deposit information for the deposit of monoclonal antibodies (mAb) 4D7, 5C5, 6B6, 8C9, 8F5, 18G4 and 24B7. Because it is not clear that cell lines possessing the properties of mAb 4D7, 5C5, 6B6, 8C9, 8F5, 18G4 and 24B7 are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of mAb 4D7, 5C5, 6B6, 8C9, 8F5, 18G4 and 24B7, a suitable deposit for patent purposes is required. Without a publicly available deposit of the above cell line, one of skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell line is an unpredictable event.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an

International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.

If the deposit has not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the hybridoma cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

7. Claims 3,6 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 3, 6, and 12 are drawn to an antibody having a binding specificity for the epitope defined by monoclonal antibodies (Mab) 1E8, 2B5, 4D7, 5C5, 6B6, 8C9, 8F5, 18G4 or 24B7. However antibodies do not have epitopes defined on them. The antigen-binding site of an antibody known as a paratope represents the site of attachment of an epitope to the antibody. Epitopes are regions on an antigen molecule that can combine with the antibody. Therefore it is unclear how an epitope is defined by the recited monoclonal antibodies. Clarification is therefore requested.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-13 and 21-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 8-15 of U.S. Patent No. 5,753,504. Although the conflicting claims are not identical, they are

not patentably distinct from each other because the instant claims are drawn to a monoclonal antibody that immunoreacts with lipopolysaccharide binding protein (LBP) but does not substantially inhibit LBP binding the LPS; the LBP is human LBP; the monoclonal antibody is one of the recited antibodies; the monoclonal antibody inhibits LBP-mediated binding of LPS to CD14; inhibits LBP-mediated LPS dependant activation of myeloid cells; a hybridoma cell line that produces the monoclonal antibody; and a pharmaceutical composition comprising the antibody.

The claims of US Patent 5,753,504 recite claims are drawn to a monoclonal antibody that immunoreacts with lipopolysaccharide binding protein (LBP), inhibits LBP-mediated binding of LPS to CD14, but does not substantially inhibit LBP binding the LPS; the LBP is human LBP; the monoclonal antibody is one of the recited antibodies; the monoclonal antibody; inhibits LBP-mediated LPS dependant activation of myeloid cells; a hybridoma cell line that produces the monoclonal antibody; and a pharmaceutical composition comprising the antibody.

Both the instant claims and the patented claims recite monoclonal antibodies named 1E8, 2B5 and both recited the same deposited hybridoma cell line having an accession number HB 11491.

Therefore, the monoclonal antibodies, hybridoma cell lines and pharmaceutical compositions are not patentably distinct.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-8 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Leturcq et al. Leturcq et al., teach the generation of monoclonal antibodies to human LBP and their use in the detection of LBP protein in serum. Three different epitope groups have been characterized. One monoclonal antibody 8C9 recognizes denatured LBP only. While the other two monoclonal antibodies 1E8 and 18G4 recognize native LBP and can detect LBP when it is complexed with LPS. It is noted that Leturcq et al., teach monoclonal antibodies with the same binding properties as the monoclonal antibodies claimed by the specification. Therefore, as a result of the generation of monoclonal antibodies Leturcq et al., inherently teach hybridoma cell lines that produced those monoclonal antibodies.

Therefore, Leturcq et al., teach the generation of monoclonal antibodies that immunoreact with lipopolysaccharide binding protein (LBP) but do not substantially inhibit LBP binding the LPS.

11. Claims 1-8 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Pugin et al. Pugin et al., teach LBP and Cd14 in normal human serum can be blocked by specific antibodies,. Monoclonal antibodies 1E8 and 18G4 against LBP

were immunoprecipitated (page 2745). Mabs 1E8 and 18G4 are specific for LBP and were used to show that endothelial and epithelial cell receptors for CD14-LPS complexes are distinct from receptors for LBP-LPS complexes. Therefore, the monoclonal antibodies taught by Pugin et al., allow binding between LPS and LBP yet inhibit binding between LPS and CD14.

Moreover, it is noted that all properties and characteristic associated with monoclonal antibodies are considered inherent. Such properties include the hybridoma cell lines that produced the monoclonal antibodies.

Therefore, Pugin et al., teach monoclonal antibodies that immunoreact with lipopolysaccharide binding protein (LBP) but does not substantially inhibit LBP binding the LPS.

Prior Art

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Martin et al., teach the use of monoclonal 1E8 and 18G4.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers

for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines
December 10, 2002

LYNETTE R. F. SMITH
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